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Germain, R. N., Bhattacharya, A., Dorf, M. E., and *Springer, T. E.*

The Journal of Immunology 128(3):1409-1413, 1982.

Other support: National Institutes of Health.

From the Department of Pathology, and the Laboratory of Membrane Immunochemistry, Sidney Farber Cancer Institute, Havard Medical School, Boston.

MAC-1 ANTIGEN: QUANTITATIVE EXPRESSION IN MACROPHAGE POPULATIONS AND TISSUES, AND IMMUNOFLUORESCENT LOCALIZATION IN SPLEEN

As reported in this paper, the expression and structure of Mac-1 on peritoneal resident macrophages and on macrophages elicited by different agents have been examined by immunofluorescence, quantitative site number determination and immunoprecipitation. The expression of Mac-1 has been compared to that of Ia, which shows differential expression on macrophages depending on the eliciting agent. The tissue distribution of Mac-1 has also been examined by absorption, and immunofluorescence was used to localize Mac-1 bearing cells in spleen sections. The results show that Mac-1 is expressed on all types of macrophages examined, validating the use of Mac-1 as a general marker for distinguishing macrophages from lymphocytes and suggesting that it must have a generalized role in macrophage function. Mac-1 expression cannot be detected in lymph node cells or in the periarteriolar lymphoid sheath region of spleen but is found in the marginal zone and red pulp. The results also show that Mac-1 is synthesized by macrophages and is present on the cell surface in sufficient quantity for biochemical purification and characterization.

Ho, M-K. and *Springer, T. A.*

The Journal of Immunology 128(5):2281-2286, 1982.

Other support: U. S. Public Health Service.

From the Laboratory of Membrane Immunochemistry, Sidney Farber Cancer Institute, Harvard Medical School, Boston.

ANTI-MAC-1 SELECTIVELY INHIBITS THE MOUSE AND HUMAN TYPE THREE COMPLEMENT RECEPTOR

Monoclonal antibodies (MAb) have proven to be of great value in identifying the cellular lineages and subsets that give rise to the diversity of the immune system. Recently, interest has focused particularly on the use of such antibodies to evaluate macrophage heterogeneity. In the study reported here, anti-Mac-1 (M1/70), a rat monoclonal antibody that reacts with mouse and human macrophages, polymorphonuclear leukocytes (PMNL), and natural killer cells, selectively inhibited complement receptor-mediated rosetting by murine macrophages and human PMNL. Preincubation of macrophages with anti-Mac-1 inhibits formation of rosettes with sheep erythrocytes bearing IgM antibody and murine C3 fragments. No inhibition was observed when other monoclonal antibodies that react with macrophages (such as anti-Ly5, anti-H-2, or anti-pan-leukocyte) were tested at 10-fold higher concentrations. Anti-Mac-1 did not affect macrophage Fc receptor-mediated rosetting. Erythrocytes bearing homogeneous human C3 fragments C3b (EC3b) or C3bi (EC3Bi) were used to test the specificity of the murine macrophage and human PMNL complement receptor inhibited by anti-Mac-1. In both cases, anti-Mac-1 inhibited CR_3-mediated rosetting of EC3bi but not CR_1-dependent rosetting of EC3b. The results show that Mac-1 is either identical to CR_3 or closely associated with CR_3 function. This is one of the first cases in which a monoclonal antibody-defined differentiation antigen has been associated with a specific cell surface function.

Beller, D. I., *Springer, T. A.* and Schreiber, R. D.

Journal of Experimental Medicine 156:1000-1009, 1982.

Other support: National Institutes of Health, American Heart Association and the American Cancer Society.

From the Department of Pathology, and the Laboratory of Membrane Immunochemistry, Sidney Farber Cancer Institute, Harvard Medical School, Boston, and the Department of Molecular Immunology, Research Institute of Scripps Clinic, La Jolla, CA.

MONOCLONAL ANTIBODIES SPECIFIC FOR RAT IgG1, IgG2a, AND IgG2b SUBCLASSES, AND KAPPA CHAIN MONOTYPIC AND ALLOTYPIC DETERMINANTS: REAGENTS FOR USE WITH RAT MONOCLONAL ANTIBODIES

A set of monoclonal antibodies (MAb) defining rat heavy chain subclasses and kappa chain monotypic and allotypic determinants was characterized in this study. Specifically, mouse monoclonal antibodies to rat IgG were obtained by fusion of immune SJL mouse spleen cells to NSI myeloma cells. Seven monoclonal antibodies were labeled with ^{125}I and studied as to specificity and avidity by using a panel of rat monoclonal antibodies both as inhibitors and target antigens in soft well plate and indirect cell binding assays. All MAb were selected for high avidity of 4×10^7 to $\geq 2 \times 10^9$ M^{-1}. Four MAb were subclass-specific, RG11/39, RG7/1, and RG7/11 were absolutely specific for the Fc′ region of IgGl, IgG2a, and IgG2b, respectively. RG9/6 showed specificity for the Fab′ region of IgG2a but cross reacted with lower avidity with IgG2c. Three MAb reacted with rat kappa chains. RG7/9 defined a monotypic (common) kappa chain determinant. RG11/15 and RG7/7 were specific for allelic

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Springer, T. A. et al.

Hybridoma 1(3):257-271, 1982

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From the Laboratory of Memb
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Other support: U. S. Public H

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kappa 1a and kappa 1b determinants, respectively. The monotypic and kappa 1a allotypic determinants are topographically separated. The antibodies can be used as screening reagents in indirect cell binding assays. They have sensitivity similar to affinity-purified rabbit anti-rat IgG and more defined specificity. They do not crossreact with mouse or human IgG, making them particularly suitable companion reagents for rat anti-mouse or anti-human MAb. One MAb, RG7/7, strongly crossreacts with Syrian hamster IgG.

Springer, T. A. et al.

Hybridoma 1(3):257-271, 1982.

Other support: U. S. Public Health Service and the American Cancer Society.

From the Laboratory of Membrane Immunochemisty, Sidney Farber Cancer Institute, Harvard Medical School, Boston.

EXPRESSION AND INDUCTION *IN VITRO* OF MACROPHAGE DIFFERENTIATION ANTIGENS ON MURINE CELL LINES

Differentiation is a process involving the coordinated control of many genes to produce different cell types. Some of these changes affect the cell surface. To follow up on this, macrophage antigens were studied on 12 macrophage cell lines and variant clones, as well as on 11 other lines representative of a variety of hematopoietic lineages, to determine the relation of surface antigen expression to cell differentiation, maturation, and function. Biosynthetic labeling followed by immunoprecipitation with monoclonal antibodies and gel electrophoresis showed that Mac-1 polypeptides of 95,000 and 170,000 M_r and the Mac-2 polypeptide of 32,000 M_r were found in lysates of mature macrophage lines but not in other lines, including myeloid or immature leukemias. The Mac-3 antigen was found in large amounts in all macrophage lines and to lesser degrees in some myeloid and B lymphoid lines. The M_r of Mac-3 varied from 100,000 to 170,000, perhaps due to differential glycosylation. Analysis of Mac-1 and Mac-2 antigens by flow cytometry showed expression on all macrophages lines. Similarly, all three Mac antigens were detected in high amounts on macrophage lines by ^{125}I-labeled antibody binding. Mac-1 and Mac-2 were not routinely seen on other hematopoietic lines, but Mac-3 was expressed in variably low amounts on some lines of myeloid and B cell lineage. Mac-1 and Mac-3 but not Mac-2 could be induced in the M1 myeloblast line by corticosteroid, lipopolysaccharide, and several conditioned media containing myeloid colony-stimulating activity. Although anti-Mac-1 does not block the detection of Mac-3 antigen on induced M1 cells, the presence of anti-Mac-1 antibody during induction partially blocked the appearance of Mac-3 antigen. Thus, the surface structure associated with Mac-1 appears to be involved in differentiation of macrophages.

Ralph, P., Ho, M-K., Litcofsky, P. B., and *Springer, T. A.*

The Journal of Immunology 130(1):108-114, 1983.

Other support: U. S. Public Health Service and the American Cancer Society.

From the Department of Developmental Hematopoiesis, Memorial Sloan-Kettering Cancer Center, Rye, NY, and the Laboratory of Membrane Immunochemistry, Sidney Farber Cancer Institute, Harvard Medical School, Boston.

QUANTITATION OF HYBRIDOMA IMMUNOGLOBULINS AND SELECTION OF LIGHT-CHAIN LOSS VARIANTS

In immunoglobulin-synthesizing cells, the genes for immunoglobulin heavy and light chains are expressed by one chromosome each, and the expression of allelic genes on the homologous chromosomes are excluded. In hybridoma cells, the active genes for immunoglobulin synthesis from both the myeloma and spleen cell parents continue to be expressed. Thus, two different heavy chains and two different light chains may be made by a single hybridoma cell. When compared to conventional antisera, hybridoma antibodies offer many advantages including specificity, consistency, availability in large quantities, and the ability to use impure immunogens. Hybridoma antibodies also differ in two other respects from conventional antibodies. First, some hybridomas secrete myeloma as well as specific antibody chains. Methods are described in Section I for selecting variant clones from mouse-rat or mouse-mouse hybrids that secrete homogenous immunoglobulins. Second, in addition to measuring antibody activity, it is often desired to measure monoclonal antibody immunoglobulin concentration. The specific antibody component of monoclonal antibodies consists of a single heavy-chain subclass and light-chain isotype. Monoclonal antibodies therefore express only a portion of the antigenic determinants found in whole immunoglobulins. This has important implications for the measurement of monoclonal immunoglobulin concentration by immunoassay. Section II describes methods for measuring rat or mouse monoclonal immunoglobulins derived from rat-mouse, mouse-mouse, or rat-rat hybrids.

Springer, T. A.

Methods in Enzymology 92:147-160, 1983.

Other support: U. S. Public Health Service and the American Cancer Society.

From the Laboratory of Membrane Immunochemistry, Sidney Farber Cancer Institute, Harvard Medical School, Boston.

MONOCLONAL ANTIBODIES AS TOOLS FOR THE STUDY OF MONONUCLEAR PHAGOCYTES

The analysis of complex biological systems has been given great impetus recently by the myeloma X immune spleen hybrid technique of Köhler and Milstein. If, for example, mouse macrophages are injected into the rat, the resultant multispecific response to a large array of different macrophage surface molecules may be resolved by cloning into a set of hybrid lines, each secreting a monoclonal antibody (MAb) recognizing a single antigenic determinant on a single cell surface molecule. Recently, a substantial number of antimacrophage MAb have been obtained that are already proving to be invaluable reagents of extraordinary specificity for the study of macrophage differentiation, function and surface antigen structure. The properties of monoclonal antibodies defining murine and human macrophage differentiation antigens are summarized in two tables presented in this report. Most antibodies have been characterized for expression on different leukocytes and cell lines, but not on nonhematopoietic tissues or on mononuclear phagocytes other than macrophages. None of these monoclonals binds to lymphocytes except 2.4G2, directed to the Fc receptor II, which

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Springer, T. A.

In: Adams, D., Edelson, P. and Koren, H. (eds.): *Methods for Studying Mononuclear Phagocytes*, New York: Academic Press, Inc., 1981, pp. 305-313.

Other support: U. S. Public Health Service.

From the Laboratory of Membrane Immunochemistry, Sidney Farber Cancer Institute, Harvard Medical School, Boston.

TISSUE DISTRIBUTION, STRUCTURAL CHARACTERIZATION, AND BIOSYNTHESIS OF MAC-3, A MACROPHAGE SURFACE GLYCOPROTEIN EXHIBITING MOLECULAR WEIGHT HETEROGENEITY

The cell distribution and biochemical characterization of the antigen, Mac-3 are described in this paper. Mac-3 is a mouse macrophage differentiation antigen defined by a rat anti-mouse monoclonal antibody (MAb), M3/84. The structure, biosynthesis, quantitative surface expression, and distribution of Mac-3 have been studied by radiolabeling and isolation with MAb-Sepharose, saturation binding, absorption, and immunofluorescence flow cytometry. In sodium dodecyl sulfate-polyacrylamide gel electrophoresis, Mac-3 migrates as a diffuse band with average M_r = 110,000. Labeling of intact cells with ^{125}I and accessibility to MAb show it is present at least in part on the cell surface. Saturation labeling with ^{125}I-MAb shows 4.2×10^4 cell surface sites on thioglycollate medium-elicited peritoneal macrophages. [^{35}S]Methionine and [^{3}H]glucosamine incorporation into Mac-3 by purified macrophages show it is a glycoprotein synthesized by these cells. Absorption shows Mac-3 is strongest in macrophages, present in lower quantities in lung, liver, bone marrow and spleen, and undetectable in thymus, lymph node, brain, and heart. Immunofluorescent flow cytometry shows surface expression on thioglycollate-elicited macrophages but not bone marrow, spleen, lymph node or thymus cell suspensions. Similar amounts of Mac-3 are immunoprecipitated from resident macrophages or macrophages elicited by sterile inflammatory agents, intracellular parasites, or immunomodulators, but the average M_r of Mac-3 varies from 92,000 to 110,000. Mac-3 is synthesized from precursor(s) of M_r = 74,000 and 79,000, identical in the different macrophages. Processing into the mature molecules occurs in 15 to 30 min.

Ho, M-K. and *Springer, T. A.*

The Journal of Biological Chemistry 258(1):636-654, 1983.

Other support: U. S. Public Health Service.

From the Laboratory of Membrane Immunochemistry, Sidney Farber Cancer Institute, Harvard Medical School, Boston.

1002319007

DISTRIBUTION OF ACTIN IN SPREADING MACROPHAGES: A COMPARATIVE STUDY ON LIVING AND FIXED CELLS

The spreading of macrophages on a substrate apparently involves changes in the distribution of several contractile and cytoskeletal proteins as revealed by immunofluorescence and electron microscopy. In the paper presented here, the distribution of actin in proteose peptone-elicited murine peritoneal macrophages is examined with fluorescent analog cytochemistry (FAC), immunofluorescence, and electron microscopy (EM). Results show, in summary, that the optimal approach for elucidating the distribution of cytoskeletal and contractile proteins involved in motile processes is a combination of three techniques. Immunofluorescence and electron microscopy can yield a great deal of information concerning the structural components of the cytoskeleton, while FAC allows the researchers to follow dynamic changes of both the soluble and structural pools of cytoskeletal proteins in living, functional cells. Results from one technique must be interpreted with caution due to the potential artifacts and limitations of each technique. The concomitant use of FAC and immunofluorescence can minimize artifacts such as local differences in pathlengths and accessible volume, thereby permitting qualitative determinations of the local concentrations of proteins in different regions of the cell.

Amato, P. A., Unanue, E. R. and *Taylor, D. L.*

The Journal of Cell Biology 96:750-761, 1983.

Other support: National Institutes of Health.

From the Department of Cellular and Developmental Biology, Harvard University, the Biological Laboratories, Cambridge, MA, and the Department of Pathology, Harvard Medical School, Boston.

PROSTAGLANDINS MODULATE MACROPHAGE Ia EXPRESSION

Prostaglandins (molecules derived from arachidonic acid of membrane lipids) are important modulators of inflammation and of humoral and cellular responses. In order to evaluate a possible mechanism for the regulation of immune responses, the effects of prostaglandins on the expression of I-region-associated (Ia) glycoproteins by macrophages have been studied. The expression of these glycoproteins is essential for macrophages to function as antigen-presenting cells during the induction of immune responses. The synthesis and membrane expression of Ia, however, is not a constitutive property of the phagocyte but is under regulation and a positive regulation of this process is exhibited by activated T cells. In contrast, a negative regulation is conspicuously found in the neonate where a product from a young replicating macrophage inhibits the expression of Ia by the mature macrophages. It is shown here that prostaglandins of the E series (PGE) are potent inhibitors of the expression of Ia-antigens on macrophages and that thromboxane B_2 antagonizes the effect of PGE.

Snyder, D. S., Beller, D. I. and *Unanue, E. R.*

Nature 299(5879):163-165, 1982.

Other support: National Institutes of Health.

From the Department of Pathology, Harvard Medical School, Boston.

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CORTICOSTEROIDS INHIBIT MURINE MACROPHAGE Ia EXPRESSION AND INTERLEUKIN 1 PRODUCTION

Corticosteroids have a broad range of effects on the tissue distribution and/or function of immunocompetent cells involved in the induction of immune responses. The investigators have now examined their effects on macrophage expression of I region-associated (Ia) molecules and production of interleukin 1 (IL 1), which are proteins required for antigen presentation and stimulation of T cells – processes essential for inducing responses to all polypeptide antigens. The major findings are that corticosteroids inhibited macrophage Ia expression, production of IL 1, and in accordance with these effects, the presentation of antigen for T cell proliferation. Lymphokine-induced Ia expression was inhibited both at the cellular level *in vitro* and at the population level *in vivo* by therapeutic doses of these drugs. In summary, corticosteroids have profound effects on functions of the macrophage associated with antigen presentation to T cells. The drugs inhibited the expression of surface I-region-associated (Ia) antigens by peritoneal macrophages both *in vitro* and *in vivo*, reduced the production of IL 1, and inhibited antigen presentation for T cell proliferation by macrophages. The doses of hydrocortisone and prednisolone that inhibited by 50% Ia expression in cultured macrophages ranged around 2 to 5 $\times 10^{-8}$M. These results could explain one mechanism by which corticosteroids suppress the induction of immune responses.

Snyder, D. S. and *Unanue, E. R.*

The Journal of Immunology 129(5):1803-1805, 1982.

Other support: National Cancer Institute.

From the Department of Pathology, Harvard Medical School, Boston.

LIGAND-INDUCED CAPPING OF SURFACE PROTEINS ON TRIFLUOPERAZINE-TREATED MACROPHAGES

Peritoneal exudate macrophages directly endocytose cross-linked membrane proteins such as Con A receptors and histocompatibility proteins. Under identical conditions, lymphocytes and transformed macrophages cap these proteins. In the experiments presented here, it could be seen that macrophages endocytosed their membrane proteins after cross-linking. After treatment with trifluoperazine, a calmodulin antagonist which inhibits endocytosis, a proportion of macrophages capped their membrane proteins. With some ligands there appeared to be a concentration threshold which was necessary to initiate capping.

Woda, B. A. and McFadden, M. L.

Experimental Cell Research 140:447-454, 1982.

Other support: From the Department of Pathology, University of Massachusetts Medical Center, Worcester.

LATERAL MOBILITY AND CAPPING OF RAT LYMPHOCYTE MEMBRANE PROTEINS

Lymphocyte membrane proteins undergo polar migration or capping after cross-linking by antibodies. There are two separable types of membrane proteins based on their capping characteristics. The prototype of one class is surface immunoglobulin (SIg) which caps after binding of a single cross-linking ligand. RT1 (rat histocompatibility proteins) and thy-1 are members of a second class of integral membrane proteins which cap only after the addition of a second ligand. In this study, fluorescence recovery after photobleaching experiments shows that there is heterogeneity in the diffusion characteristics of lymphocyte membrane proteins. SIg is relatively immobile when labeled by Fab' and is immobilized by $F(ab')_2$. RT1 diffuses 2.7 times as fast as SIg and the mobile fraction of RT1 is greater. When RT1 is cross-linked by relatively low concentrations of $F(ab')_2$ its mobility is about the same as that of SIg. When the concentration of $F(ab)_2$ is increased, RT1 is immobilized. Thy-1 diffuses faster than SIg and has a higher mobile fraction. When thy-1 is labeled with $F(ab')_2$ it remains mobile and is immobilized when a second antibody layer is added. The data presented here show that while there appear to be only two classes of lymphocyte membrane protein capping, the lateral mobility of membrane proteins is more heterogeneous. The relative order of lateral mobility of membrane proteins is thy-1 >>RT1 >SIg.

Woda, B. A. and Gilman, S. C.

Cell Biology International Reports 7(3):203-209; 1983.

Other support: National Institutes of Health.

From the Department of Pathology, University of Massachusetts Medical Center, Worcester, and the Research Institute of Scripps Clinic, La Jolla, CA.

VII. *Epidemiology*

INFLUENCE OF CIGARETTE, PIPE, AND CIGAR SMOKING, REMOVABLE PARTIAL DENTURES, AND AGE ON ORAL LEUKOPLAKIA

In this epidemiological study, 925 healthy male subjects from the Veterans Administration Dental Longitudinal Study were examined for oral leukoplakia lesion site and prevalence. The participants were grouped according to smoking status: nonsmokers, smokers of cigarettes, cigars, pipe, or cigarettes plus another tobacco product. In addition, the amount of product smoked, presence of a removable partial denture, and age were examined to determine their relation to leukoplakia. Results showed that leukoplakia lesions existed in 127 (13.7%) of the total 925 persons. The 443 nonsmokers had a prevalence of 3.8%; the 482 total smokers had a lesion prevalence of 22.8%. Furthermore, the data indicated that cigar smokers had significantly fewer lesions than the other smoker groups and that persons smoking a pipe or a pipe plus cigars had the highest prevalence. Heavy cigarette smokers had significantly more palatal lesions than light to moderate cigarette smokers. While removable partial dentures did not

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Baric, J. M. *et al.* (*Bossé, R*

Oral Surgery 54(4):424-429,

Other support: Medical Res

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sons. The 443 nonsmok-
on prevalence of 22.8%.
cantly fewer lesions than
a pipe plus cigars had the
tly more palatal lesions
partial dentures did not

appear to affect lesion prevalence significantly, older smokers, persons of 50 years and above, had a significantly higher prevalence than persons less than 50 years of age.

Baric, J. M. *et al.* (*Bossé, R.*)

Oral Surgery 54(4):424-429, 1982.

Other support: Medical Research Service of the Veterans Administration.

From the Veterans Administration Outpatient Clinic and Harvard School of Dental Medicine, Boston.

A CROSS-NATIONAL EPIDEMIOLOGICAL RESOURCE: THE SWEDISH AND FINNISH COHORT STUDIES OF LIKE-SEXED TWINS

In 1961 a nationwide registry of 12,889 like-sexed twin pairs born between 1886 and 1925 was set up in Stockholm, Sweden; in 1973 this registry was extended to include like-sexed twin pairs born between 1926 and 1958. In 1974, a study of 17,357 like-sexed twin pairs born before 1958 and alive in 1967 was started in Helsinki, Finland. Both studies comprise an unselected series that has been studied in a comparable fashion. Zygosity determination and health questionnaire data-gathering were carried out in 1973 for the Swedish study and in 1975 for the Finnish study for the comparable age groups. Data on hospital usage, cancer incidence and mortality are collected by record-linkage from the respective national registries. Cross-national twin studies can permit testing of hypotheses of the relationships between genetic and cultural factors and major chronic diseases and their risk factors. Specifically, an immediate objective of this study is to present descriptive results relating to disease symptoms and behavioral characteristics for Sweden and Finland. Then the data collected can be used to estimate the importance of different environmental risk factors and genotype in explaining differences in morbidity and mortality between the two countries.

Cederlöf, R. *et al.* (*Rantasalo, I.* and *Floderus-Myrrhed, B.*)

International Journal of Epidemiology 11(4):387-390, 1982.

Other support: From the Department of Public Health Science, University of Helsinki, and the Department of Environmental Hygiene of the Karolinska Institutet and the National Institute of Environmental Medicine, Stockholm.

CIGARETTE SMOKING AND ALCOHOL USE IN FINLAND AND SWEDEN: A CROSS-NATIONAL TWIN STUDY

Finland and Sweden both have twin cohort studies. In this cross-national twin study, cigarette smoking and alcohol use in Finland and Sweden were compared using data from the two studies on like-sexed adult twin pairs aged 18-47 (total of 20,056 pairs). Results showed that Finnish men were heavier consumers of tobacco and alcohol than Swedish men. When heavy consumers (>500g of alcohol/month and >20 cigarettes/day) were considered, the prevalence rate was 9.7% in Finnish men and 5.1% in Swedish men. Since there is a higher morbidity in Finland than in Sweden

from many smoking- and alcohol-associated diseases, this difference might account for it. Genetic factors in smoking and alcohol use were assessed by comparing observed and expected coincidence rates, and by multivariate analyses. Genetic and familial effects were defined as an excess coincidence in monozygotic pairs compared to dizygotic (DZ) pairs, and by an increased DZ coincidence rate compared to that expected. Significant genetic and familial effects were observed for cigarette smoking and for smoking more than one pack of cigarettes a day. Significant familial effects for alcohol use were observed and a significant genetic effect was obtained for men. However, a significant genetic effect could not be observed for the combined heavy use of alcohol and heavy smoking. The genetic and familial effects seemed to be mostly independent of country and sex.

Kaprio, J. *et al.* (*Rantasalo, I.* and *Floderus-Myrrhed, B.*)

International Journal of Epidemiology 11(4):378-386, 1982.

Other support: From the Department of Public Health Science, University of Helsinki, and the Department of Environmental Hygiene of the Karolinska Institutet and the National Institutet of Environmental Medicine, Stockholm.

A SEMANTIC DIFFERENTIAL OF PSYCHOSOCIAL BEHAVIOUR PATTERNS

A behavioral self-assessment rating scale developed for use in questionnaire studies can also be used to assess characteristics of other persons well-known to the self (siblings, spouse, cotwin, etc.). The method used to construct the 43-item scale was the semantic differential technique. After a pilot sutdy was run using this scale, a slightly revised version was administered to six groups of working-aged persons in the Helsinki area (n = 238). The subjects' age, sex, occupation, educational level as well as education and occupation of their parents were recorded. A varimax-rotated factor analysis indicated that four factors could be identified with characteristic values >1.0. These factors, named according to the positive end of the reading, were: (1) spontaneity-openness, (2) self-control-calmness, (3) self-confidence-dominance, and (4) conscientiousness-responsibility. Analysis of covariance of the factor scores with background variables as independent variables showed that sex was the only significant explanatory variable for the first, second and fourth factors. A shortened version of the scale was constructed using the five items with the highest loadings on each factor. Item analyses yielded reliability estimates of 0.81, 0.77, 0.82, and 0.68 for the four shortened factor scales. Thus, a reliable behavioral self-assessment scale with four dimensions was developed that is based on using everyday words in a semantic differential. The factor structures seem to be independent of educational and occupational factors, but sex differences for three of the four scales were observed. This instrument, which has been used in the 1979 and 1981 questionnaire studies of the Finnish Twin Cohort Study, will continue to be used as a behavioral assessment tool in clinical and epidemiological studies.

Langinvainio, H. *et al.* (*Rantasalo, I.*)

Kansanterveystieteen julkaisuja M 68:1-43, 1982.

Other support: From the Department of Public Health Science, University of Helsinki.

HEREDITARY AND EI SLEEP LENGTH

An earlier survey c difference in sleep lengtl though it is known that limited, it is difficult to biological factors, while virtually unknown. In th length, the authors have c and dizygotic (DZ) twin: consists of all adult like-s members alive and answ mined by questionnaire v 4,545 DZ. 1,328 of the p night sleep was 7 h 51 mi sexes and different age females averaged 11 min n DZ twin pairs living tog showing cohabitation to influenced by age and sex the latter factors were ass parameter. For short slee zygosity, cohabitation an long sleep (≥ 9 h) signific Self-reports on sleep lengt a constellation of undefine Thus, for example, in me to sleep quality and incom influenced by age and env genetic and possibly othe

Partinen, M. *et al.* (*Rant*

In: Proceedings of the 6th Basel: Karger, 1983, pp.

Other support: Finnish C

From the Departments of sity of Helsinki.

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:, University of Helsinki.

HEREDITARY AND ENVIRONMENTAL DETERMINATION OF HUMAN SLEEP LENGTH

An earlier survey on self-reported sleep characteristics has shown a definite difference in sleep length between Finnish and corresponding American youths. Although it is known that normative data on human sleep length are geographically limited, it is difficult to assess to what extent such differences reflect cultural and biological factors, while the genetic determinants of normal sleep in humans are virtually unknown. In this attempt to estimate the role of genetic factors on sleep length, the authors have compared the self-reported sleep length in monozygotic (MZ) and dizygotic (DZ) twins of the Finnish twin cohort study. The material used here consists of all adult like-sexed Finnish twin pairs ($n = 11,368$) born before 1958, both members alive and answering a questionnaire mailed in 1975. Zygosity was determined by questionnaire validated by blood sampling. 2,237 of the pairs were MZ and 4,545 DZ. 1,328 of the pairs lived together. Results showed that the overall mean of night sleep was 7 h 51 min. There were small but significant differences between the sexes and different age groups. Sex difference was greatest at 20-34 years when females averaged 11 min more sleep than males. Intraclass correlations for both MZ and DZ twin pairs living together were expectedly higher than for those living apart, showing cohabitation to be an important synchronizing factor. As cohabitation was influenced by age and sex, which also affected sleep, the relative roles of genetic and the latter factors were assessed by multivariate logit analysis for concordance of each parameter. For short sleep (≥ 6 h) the logit analysis indicated significant effects for zygosity, cohabitation and age, with a significant interaction between age and sex. For long sleep (≥ 9 h) significant effects were detected for zygosity, cohabitation and sex. Self-reports on sleep length show individual differences, which have been attributed to a constellation of undefined biophysiological, psychosocial and environmental factors. Thus, for example, in men of the present study population sleep length was correlated to sleep quality and income. These results indicate that whereas human sleep is greatly influenced by age and environment, one-third of the variance in sleep length is due to genetic and possibly other factors that make MZ twins more similar than DZ twins.

Partinen, M. *et al.* (*Rantasalo, I.*)

In: Proceedings of the 6th European Congress on Sleep Research, Zurich, 1982: *Sleep*, Basel: Karger, 1983, pp. 206-208.

Other support: Finnish Cultural Foundation.

From the Departments of Neurology, Physiology and Public Health Science, University of Helsinki.

Active Projects

Following is a list of the principal investigators, or institutions, of projects under way or activated in the period since the previous Report, together with the respective project titles. Completed projects are listed in a later section.

PRINCIPAL INVESTIGATOR OR INSTITUTION	PROJECT TITLE
LEO G. ABOOD, PH.D., *Professor of Brain Research and Biochemistry,* Center for Brain Research, University of Rochester Medical Center, Rochester, NY.	Nicotine transfer-disposition in liver cells
KENNETH B. ADLER, PH.D., *Assistant Professor of Pathology,* University of Vermont College of Medicine, Burlington.	Airway mucin secretion: effects of products from bacteria associated with chronic bronchitis
JOHN J. ALBERS, PH.D., *Research Associate Professor of Medicine,* University of Washington School of Medicine, Seattle.	High density lipoprotein quantitation
HARRY N. ANTONIADES, PH.D., *Professor of Biochemistry,* Harvard University School of Public Health, Boston.	Human platelet-derived growth factor (PDGF): relationship to human atherosclerosis
THOMAS M. AUNE, PH.D., *Adjunct in Immunology,* The Jewish Hospital of St. Louis.	Interferon—activation of suppressor T cell pathways
BERNARD M. BABIOR, M.D., PH.D., *Professor of Medicine,* New England Medical Center Hospital, Boston.	Studies on the mechanism of activation of the respiratory burst in neutrophils
LESLIE BAER, M.D., *Associate Professor of Medicine,* Columbia University College of Physicians & Surgeons, New York.	Cigarette smoking in normotensive and hypertensive subjects: blood pressure, renin, aldosterone and catecholamine responses
SAMUEL BALK, M.D., PH.D., *Pathologist,* New England Deaconess Hospital, Boston.	Serum mitogens, hormones, ions, viral transforming genes and tumor reversal in appropriate and autonomous initiation of cell replication
RICHARD J. BING, M.D., *Professor of Medicine (emeritus);* University of Southern California School of Medicine, Los Angeles; *Visiting Associate,* California Institute of Technology; *Director of Experimental Cardiology and Scientific Development,* Huntington Medical Research Institute, Pasadena, CA.	Lipoproteins and the arterial wall
DEBAJIT K. BISWAS, PH.D., D.Sc., *Associate Professor of Oral Biology,* Laboratory of Pharmacology, Harvard School of Dental Medicine, Boston.	Effects of nicotine and benzo(α)pyrene on hormone production
IRA B. BLACK, M.D., *Professor and Chief, Division of Developmental Neurology,* Cornell University Medical College, New York.	Nicotine and neuronal development
PHYLLIS B. BLAIR, PH.D., *Professor of Immunology,* University of California, Berkeley.	Regulation of natural killer cell activity

PRINCIPAL INVESTIGATOR OR INSTITUTION

EDWARD BRESNICK, PH.D., *and Chairman, Department of try,* The University of Vermont Medicine, Burlington.

VINCENZO BUONASSISI, M.D *Research Biologist,* The Univer fornia at San Diego, La Jolla.

EDWARD J. CAMPBELL, M.D *Professor of Medicine,* Washing sity School of Medicine, St. Lc

FRANCIS C. CHAO, M.D., PH *Investigator,* Center for Blood Boston.

LAN BO CHEN, PH.D., *Associat of Pathology,* Sidney Farber C tute, Boston.

JAN F. CHLEBOWSKI, PH.D. *Professor of Biochemistry,* Medi of Virginia, Richmond.

CURT I. CIVIN, M.D., *Assistant P Oncology & Pediatrics,* The Joh Oncology Center, Baltimore.

BRIAN L. CLEVINGER, PH.D. *Professor of Biomedical Science* ton University School of Dental St. Louis.

CHARLES G. COCHRANE, M *ber, Department of Immuno* Scripps Clinic and Research F La Jolla, CA.

BERNICE H. COHEN, PH.D., *Pro Director, Human Genetics/Gen miology Program,* The Johns Hc versity School of Hygiene a Health, Baltimore.

ROBERT W. COLMAN, M.D., *P Medicine,* Temple University Medicine, Philadelphia.

CARL E. CRUETZ, PH.D., *Assist sor of Pharmacology,* Universi ginia School of Medicine, Charl

GIDON CZAPSKI, M.Sc., PH.D., *of Physical Chemistry,* The Hebr sity, Jerusalem, Israel.

ALBERT B. DEISSEROTH, M.I *Professor of Medicine,* Veterans tration Medical Center, San Fra

PETER H. DUESBERG, PH.D., *P Molecular Biology,* University nia, Berkeley.

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PRINCIPAL INVESTIGATOR OR INSTITUTION	PROJECT TITLE
EDWARD BRESNICK, PH.D., *Professor and Chairman, Department of Biochemistry*, The University of Vermont College of Medicine, Burlington.	Expression of cytochrome P450c
VINCENZO BUONASSISI, M.D., *Associate Research Biologist*, The University of California at San Diego, La Jolla.	Heparan sulfate proteoglycans and blood homeostatic mechanisms
EDWARD J. CAMPBELL, M.D., *Assistant Professor of Medicine*, Washington University School of Medicine, St. Louis.	Modulators of inflammatory cell proteolytic activity
FRANCIS C. CHAO, M.D., PH.D., *Senior Investigator*, Center for Blood Research, Boston.	Platelet activation and blood hypercoagulability
LAN BO CHEN, PH.D., *Associate Professor of Pathology*, Sidney Farber Cancer Institute, Boston.	Studies on human oat cell carcinomas
JAN F. CHLEBOWSKI, PH.D., *Assistant Professor of Biochemistry*, Medical College of Virginia, Richmond.	Calorimetric investigation of proteinase-α_2-macroglobulin interaction
CURT I. CIVIN, M.D., *Assistant Professor of Oncology & Pediatrics*, The Johns Hopkins Oncology Center, Baltimore.	Biochemistry and function of human granulopoietic antigens
BRIAN L. CLEVINGER, PH.D., *Assistant Professor of Biomedical Science*, Washington University School of Dental Medicine, St. Louis.	Role of J segment in V segment expression
CHARLES G. COCHRANE, M.D., *Member, Department of Immunopathology*, Scripps Clinic and Research Foundation, La Jolla, CA.	Mediation systems in inflammatory lung disease
BERNICE H. COHEN, PH.D., *Professor and Director, Human Genetics/Genetic Epidemiology Program*, The Johns Hopkins University School of Hygiene and Public Health, Baltimore.	Genetic-epidemiologic characteristics of smokers and nonsmokers
ROBERT W. COLMAN, M.D., *Professor of Medicine*, Temple University School of Medicine, Philadelphia.	Initiation of plasma coagulation and kinin forming systems in man
CARL E. CRUETZ, PH.D., *Assistant Professor of Pharmacology*, University of Virginia School of Medicine, Charlottesville.	Role of protein phosphorylation in nicotine reduced catecholamine release
GIDON CZAPSKI, M.Sc., PH.D., *Professor of Physical Chemistry*, The Hebrew University, Jerusalem, Israel.	On the toxicity of oxygen and superoxide ion: is superoxide toxic?
ALBERT B. DEISSEROTH, M.D., PH.D., *Professor of Medicine*, Veterans' Administration Medical Center, San Francisco.	Study of altered alpha globin genes in leukemia and solid tumors
PETER H. DUESBERG, PH.D., *Professor of Molecular Biology*, University of California, Berkeley.	Transforming genes of two acute leukemia viruses

PRINCIPAL INVESTIGATOR OR INSTITUTION	PROJECT TITLE
HAROLD F. DVORAK, M.D., *Chief, Department of Pathology*, Beth Israel Hospital, Boston.	Pathogenesis of tumor desmoplasia
V. GENE ERWIN, PH.D., *Professor of Pharmacology; Dean*, University of Colorado School of Pharmacy, Boulder.	Effects of nicotine on neuropeptide secretion by intact mouse brain, a pharmacogenetic study
ALVAN R. FEINSTEIN, M.D., *Professor of Medicine & Epidemiology*, Yale University School of Medicine, New Haven, CT.	Smoking, detection bias and primary lung cancer
RICHARD FENTON, PH.D., *Instructor in Physiology*, University of Massachusetts School of Medicine, Worcester.	Physiological effects of nicotine on calcium and adenosine metabolism by the heart
THOMAS H. FINLAY, PH.D., *Associate Professor of Obstetrics and Gynecology*, New York University Medical Center, New York.	Structure, properties and regulation of mouse plasma protease inhibitors
PAUL B. FISHER, PH.D., *Senior Research Associate, Department of Microbiology*, Columbia University College of Physicians & Surgeons, New York.	Chemical-viral interactions in cell transformation
JOSEPH A. FONTANA, M.D., PH.D., *Assistant Professor of Medicine and Biochemistry*, West Virginia University Medical Center, Morgantown.	Glycosyltransferases and glycoprotein synthesis in differentiation induced phenotypic reversal of malignancy by retinoic acid cyclic nucleotides and other agents
JUDITH ANN FOSTER, PH.D., *Professor and Chairperson, Department of Biology*, Syracuse University, Syracuse, NY.	Involvement of elastin in lung disease
JACK W. FRANKEL, PH.D., *Consultant in Medical Research*, Veterans Administration Medical Center, Bay Pines, FL.	Smoking and lung cancer: diagnostic test to identify persons at high risk
ALLAN P. FREEDMAN, M.D., *Assistant Professor of Medicine*, Hahnemann Medical College, Philadelphia.	The effect of cigarette smoking on the alveolar clearance rate of inert dust particles in the human lung
AARON E. FREEMAN, PH.D., *Staff Scientist*, California Biomedical Research Foundation, La Jolla, CA.	Rodent and human lung epithelial cell culture as a tool for carcinogenesis research *in vitro*
KJELL FUXE, M.D., *Professor of Histology*, The Karolinska Institute, Stockholm.	Nicotine, catecholamines and neuroendocrine functions
JACQUES E. GIELEN, PH.D., *Associate Professor, Laboratory of Medical Chemistry, Toxicology and Hygiene*, Institute of Pathology, University of Liège, Liège, Belgium.	Modulation of aryl hydrocarbon hydroxylase and epoxide hydratase in animal tissues and in cell culture by cigarette smoke condensate and other chemicals
	Biochemical mechanism(s) and qualitative and quantitative consequences of benzo-(α)pyrene metabolism
GABRIEL C. GODMAN, M.D., *Professor of Pathology*, Columbia University College of Physicians & Surgeons, New York.	Cytoskeletal organization of the endothelial cell in regulation of shape contractility and surface movement

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WARREN M. GOLD, M.D., *Medicine*, Cardiovascular Re tute, University of California cisco.

SIDNEY GOLDFISCHER, M.D *of Pathology*, Albert Einstein Medicine, The Bronx, NY.

MAURICE GREEN, M.D., *Di tute for Molecular Virology*, S versity Medical Center, St. L

CHARLES S. GREENBERG, *ant Professor of Medicine*, Du Medical Center, Durham, NC

MARK I. GREENE, PH.D., *A fessor of Pathology*, Harv School, Boston.

NOBUYOSHI HAGINO, M.D. *fessor of Anatomy*, Univers Health Science Center, San A

CAROLINE B. HALL, M.D., *fessor of Pediatrics and Medi* sity of Rochester School Rochester, NY.

LINDA M. HALL, PH.D., *Ass sor of Genetics and Neurosc* Einstein College of Medicin University, The Bronx, NY.

PAUL HAMOSH, M.D., *Assoc of Physiology and Biophysic cine*, Georgetown Universit Medicine and Dentistry, Was

NORMAN W. HEIMSTRA, P *sor of Psychology; Director, tors Laboratory*, University kota, Vermillion

ROBERT M. HOFFMAN, PH *Professor of Pediatrics in R* versity of California School La Jolla.

JEROME L. HOJNACKI, PH *Professor of Biological Scie* sity of Lowell, Lowell, MA.

WAYNE HOSS, PH.D., *Associ* Center for Brain Research, Rochester Medical Center, R

HAROLD P. JONES, PH.D., *fessor of Biochemistry*, Univ Alabama, Mobile.

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PRINCIPAL INVESTIGATOR OR INSTITUTION	PROJECT TITLE
WARREN M. GOLD, M.D., *Professor of Medicine*, Cardiovascular Research Institute, University of California, San Francisco.	Effect of ozone on airway mast cells
SIDNEY GOLDFISCHER, M.D., *Professor of Pathology*, Albert Einstein College of Medicine, The Bronx, NY.	Extracellular matrix-cytochemistry and ultrastructure
MAURICE GREEN, M.D., *Director, Institute for Molecular Virology*, St. Louis University Medical Center, St. Louis.	Amplification of human adenovirus transformation proteins in prokaryotic and eukaryotic cells
CHARLES S. GREENBERG, M.D., *Assistant Professor of Medicine*, Duke University Medical Center, Durham, NC.	Transglutaminases and atherosclerosis
MARK I. GREENE, PH.D., *Associate Professor of Pathology*, Harvard Medical School, Boston.	Suppressor cells in syngeneic tumor immunity
NOBUYOSHI HAGINO, M.D., PH.D., *Professor of Anatomy*, University of Texas Health Science Center, San Antonio.	Nicotinic receptors of LHRH axon terminals in the median eminence
CAROLINE B. HALL, M.D., *Associate Professor of Pediatrics and Medicine*, University of Rochester School of Medicine, Rochester, NY.	Interrelationship of infectious lower respiratory tract disease in infancy, and host and environmental factors to later development of chronic lung disease
LINDA M. HALL, PH.D., *Associate Professor of Genetics and Neuroscience*, Albert Einstein College of Medicine of Yeshiva University, The Bronx, NY.	Genetic differences in nicotine sensitivity in *Drosophila melanogaster* strains
PAUL HAMOSH, M.D., *Associate Professor of Physiology and Biophysics, and Medicine*, Georgetown University Schools of Medicine and Dentistry, Washington, D.C.	Cigarette smoke and lipoprotein remodeling by the lung
NORMAN W. HEIMSTRA, PH.D., *Professor of Psychology; Director, Human Factors Laboratory*, University of South Dakota, Vermillion.	Some behavioral aspects of smoking and smoking deprivation
ROBERT M. HOFFMAN, PH.D., *Assistant Professor of Pediatrics in Residence*, University of California School of Medicine, La Jolla.	Methionine dependence, methylation and organic transformation Regulation of cellular oncogenes
JEROME L. HOJNACKI, PH.D., *Assistant Professor of Biological Sciences*, University of Lowell, Lowell, MA.	Nicotine-induced changes in primate high density lipoproteins
WAYNE HOSS, PH.D., *Associate Professor*, Center for Brain Research, University of Rochester Medical Center, Rochester, NY.	Studies of nicotine interaction with blood cells
HAROLD P. JONES, PH.D., *Assistant Professor of Biochemistry*, University of South Alabama, Mobile.	Calcium-dependent regulatory proteins and neutrophil activation

PRINCIPAL INVESTIGATOR OR INSTITUTION	PROJECT TITLE
MORRIS J. KARNOVSKY, M.B., B. CH., *Shattuck Professor of Pathological Anatomy*, Harvard Medical School, Boston.	The molecular basis of pulmonary surfactant secretion by type II pneumocytes: studies in intact cells and a cell-free system
SIMON KARPATKIN, M.D., *Professor of Medicine*, New York University Medical Center, New York.	The role of platelets in tumor cell metastases
SHIRLEY L. KAUFFMAN, M.D., *Professor of Pathology*, State University of New York Downstate Medical Center, Brooklyn.	Oncogenes in chemical carcinogenesis
INGEGERD M. KEITH, PH.D., *Assistant Professor of Anatomy*, University of Wisconsin School of Veterinary Medicine, Madison.	Part I: Lung neuroendocrine cell innervation Part II: Transplacental effect of smoking on lung neuroendocrine cells in the neonate
HEINZ KOHLER, M.D., PH.D., *Director, Department of Molecular Immunology*, Roswell Park Memorial Institute, Buffalo, NY.	Multi-targeting with hybridomas on tumor cells
MARKKU KOSKENVUO, M.D., *Assistant Professor, Department of Public Health Science*, University of Helsinki, Helsinki, Finland.	The Finnish Twin Cohort Follow-up Study
ROBERT W. KREILICK, PH.D., *Professor of Chemistry*, University of Rochester, Rochester, NY.	Investigations of the interaction of nicotine with membranes
KLAUS E. KUETTNER, PH.D., *Professor and Chairman: Department of Biochemistry*, Rush College of Health Sciences and Rush Medical College, Rush-Presbyterian-St. Luke's Medical Center, Chicago.	Regulation of proliferation of invasive cells
ABEL LAJTHA, PH.D., *Director*, New York State Research Institute for Neurochemistry and Drug Addiction, New York.	Genetic basis for nicotine response
DON LAPENAS, M.D., *Assistant Professor of Pathology*, University of Vermont College of Medicine, Burlington.	The association of inorganic dust deposition with pulmonary neoplasia in tobacco users
E. CLINTON LAWRENCE, M.D., *Assistant Professor of Medicine*, Baylor College of Medicine, Houston.	Effects of cigarette smoking on immunoglobulin production by human bronchial lymphocytes
PHILIP M. LE QUESNE, PH.D., D.SC., *Professor of Chemistry*, Northeastern University, Boston.	Assay of oxygenated sterols in human blood vessels – a feasibility study
GESINA L. LONGNECKER, PH.D., *Associate Professor of Pharmacology*, University of South Alabama College of Medicine, Mobile.	Studies of platelet and endothelial prostanoid production as possible cardiovascular risk indicators in smokers
RONALD B. LUFTIG, PH.D., *Professor and Head, Department of Microbiology and Immunology*, LSU Medical Center, New Orleans.	Interactions between RNA viruses and chemical carcinogens

PRINCIPAL INVESTIGATO
OR INSTITUTION

JAN M. LUNDBERG, M.D., *fessor of Pharmacology*, Ka tutet, Stockholm, Sweden.

HENRY T. LYNCH, M.D., *Chairman, Department of Pr cine and Public Health*, Crei sity School of Medicine, Om

BRUCE A. MACHER, PH.D., *fessor of Pharmaceutical C* versity of California, San Fr

RICHARD A. MARKHAM, M *Professor of Medicine and o and Immunology*, The Jewi St. Louis, St. Louis.

ALAN C. McLAUGHLIN, P *in Biochemistry/Biophysics*, Pennsylvania School of Me delphia.

FERID MURAD, M.D., PH.D *Medicine and Pharmacol* University, and *Chief of* Alto V.A. Hospital, Stanfor

CHRISTOPHER MURLAS, M *Professor of Medicine*, Uni fornia School of Medicine,

JAY A. NADEL, M.D., *Prof cine, Physiology and Radi* vascular Research Institute, California, San Francisco.

DONALD J. NELSON, PH. *Professor of Chemistry*, Cl Worcester, MA.

STAFAN NIEWIAROWSKI, *Professor of Physiology*, T search Center, Temple Unive Medicine, Philadelphia.

F. WILLIAM ORR, M.D., *As sor of Pathology*, Universit Winnipeg, Manitoba, Cana

BENDICHT U. PAULI, D.V *Professor of Pathology*, Rus St. Lukes Medical Center,

BORIS M. PETERLIN, M.D. *fessor of Medicine*, Sectio tology-Clinical Immunolog California School of Medic cisco.

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PRINCIPAL INVESTIGATOR OR INSTITUTION	PROJECT TITLE
JAN M. LUNDBERG, M.D., *Assistant Professor of Pharmacology*, Karolinska Institutet, Stockholm, Sweden.	Sensory neuropeptides and smoke-induced irritation in the respiratory tract
HENRY T. LYNCH, M.D., *Professor and Chairman, Department of Preventive Medicine and Public Health*, Creighton University School of Medicine, Omaha.	Genetic and biomarker studies of cancers of the respiratory tract, pancreas and urinary bladder
BRUCE A. MACHER, PH.D., *Assistant Professor of Pharmaceutical Chemistry*, University of California, San Francisco.	Chemistry and biology of complex carbohydrates
RICHARD A. MARKHAM, M.D., *Assistant Professor of Medicine and of Microbiology and Immunology*, The Jewish Hospital of St. Louis, St. Louis.	T cell-mediated immunity to *Pseudomonas aeruginosa*
ALAN C. McLAUGHLIN, PH.D., *Lecturer in Biochemistry/Biophysics*, University of Pennsylvania School of Medicine, Philadelphia.	Interaction of divalent cations with model and biological membranes
FERID MURAD, M.D., PH.D., *Professor of Medicine and Pharmacology*, Stanford University, and *Chief of Medicine*, Palo Alto V.A. Hospital, Stanford, CA.	Mechanism of nitric oxide activation of guanylate cyclase Role of cyclic GMP in smooth muscle relaxation
CHRISTOPHER MURLAS, M.D., *Assistant Professor of Medicine*, University of California School of Medicine, Irvine.	Airway muscle abnormalities in bronchial hyperreactivity
JAY A. NADEL, M.D., *Professor of Medicine, Physiology and Radiology*, Cardiovascular Research Institute, University of California, San Francisco.	Mechanisms of airway hyperreactivity
DONALD J. NELSON, PH.D., *Associate Professor of Chemistry*, Clark University, Worcester, MA.	Interaction of cholinergic ligands with genetic variants of the acetylcholine receptor
STAFAN NIEWIAROWSKI, M.D., PH.D., *Professor of Physiology*, Thrombosis Research Center, Temple University School of Medicine, Philadelphia.	Platelet interaction with fibrinogen and its significance in hemostasis
F. WILLIAM ORR, M.D., *Associate Professor of Pathology*, University of Manitoba, Winnipeg, Manitoba, Canada.	Role of local factors in pulmonary metastasis
BENDICHT U. PAULI, D.V.M., *Associate Professor of Pathology*, Rush Presbyterian-St. Lukes Medical Center, Chicago.	Local regulation of tumor invasion by host-derived proteinase inhibitors
BORIS M. PETERLIN, M.D., *Assistant Professor of Medicine*, Section of Rheumatology-Clinical Immunology, University of California School of Medicine, San Francisco.	Biology and molecular biology of the differentiation of a human monocytoid cell line